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08/398,555	03/03/1995	LINDA G. CIMA	MIT6210	7254
23579	7590	10/03/2003	EXAMINER	
PATREA L. PABST HOLLAND & KNIGHT LLP SUITE 2000, ONE ATLANTIC CENTER 1201 WEST PEACHTREE STREET, N.E. ATLANTA, GA 30309-3400			RUSSEL, JEFFREY E	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

## Application No.

08/398,555

## Applicant(s)

CIMA ET AL.

## Examiner

Jeffrey E. Russel

## Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 14-17 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-17 and 32-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 21 July 1997 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 14-17 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,906,828 and further in view of Nitecki et al, Kausch et al, and Applicants' admission of the prior art at page 12, lines 1-12, of the specification. Although the conflicting claims are not identical, they are not patentably distinct from each other. It is the examiner's position that a one-way test is appropriate for obviousness-type double patenting. The claims of the '828 patent do not recite using the same attachment agent to link the tether to the substrate and the growth effector molecule. Nitecki et al (see, e.g., column 1, line 67 - column 2, line 15) and Kausch et al (see, e.g., column 6, lines 52-67) disclose that homobifunctional coupling agents and linkers are known for purposes of coupling of biological materials and for immobilization, albeit having the disadvantage of intramolecular cross-linking and self-condensation and the loss of a portion of the linker due to reaction of both ends of the linker with the support. It would have been obvious to one of ordinary skill in the art to use the same attachment agent to link the tether to the substrate and the growth effector molecule in the claimed invention of the '828 patent, with only the expected disadvantages arising from the use of homobifunctional rather than

heterobifunctional coupling agents or linkers, because the claims of the '828 patent require covalent attachment yet are not limited to any particular attachment agents, because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan, and because Nitecki et al and Kausch et al teach that the use of homobifunctional coupling agents and linkers are known and useful in the art for the same purpose claimed in the '828 patent. The claims of the '828 patent do not recite an attachment agent which is cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, or maleimide. Applicants admit at page 12, lines 1-12, of the specification that cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides are standard immobilization chemistries which are well known in the art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to attach the tethers recited in the claimed invention of the '828 patent to the substrate using standard immobilization chemistries which are well known in the art, including cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides, because the claims of the '828 patent require covalent attachment yet are not limited to any particular attachment agents and because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan.

3. Claims 32 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 20 of U.S. Patent No. 6,045,818 and further in view of Nitecki et al, Kausch et al, and Applicants' admission of the prior art at page 12, lines 1-12, of the specification. Although the conflicting claims are not identical, they are not patentably

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distinct from each other. It is the examiner's position that a one-way test is appropriate for obviousness-type double patenting. The claims of the '818 patent do not recite using the same attachment agent to link the tether to the substrate and the growth effector molecule. Nitecki et al (see, e.g., column 1, line 67 - column 2, line 15) and Kausch et al (see, e.g., column 6, lines 52-67) disclose that homobifunctional coupling agents and linkers are known for purposes of coupling of biological materials and for immobilization, albeit having the disadvantage of intramolecular cross-linking and self-condensation and the loss of a portion of the linker due to reaction of both ends of the linker with the support. It would have been obvious to one of ordinary skill in the art to use the same attachment agent to link the tether to the substrate and the growth effector molecule in the claimed invention of the '818 patent, with only the expected disadvantages arising from the use of homobifunctional rather than heterobifunctional coupling agents or linkers, because the claims of the '828 patent require covalent attachment yet are not limited to any particular attachment agents, because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan, and because Nitecki et al and Kausch et al teach that the use of homobifunctional coupling agents and linkers are known and useful in the art for the same purpose claimed in the '828 patent. The claim of the '818 patent does not recite an attachment agent which is cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, or maleimide. Applicants admit at page 12, lines 1-12, of the specification that cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides are standard immobilization chemistries which are well known in the art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made

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to attach the tethers recited in the claimed invention of the '818 patent to the substrate using standard immobilization chemistries which are well known in the art, including cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides, because the claims of the '818 patent require covalent attachment yet are not limited to any particular attachment agents and because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 14-16 and 33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herweck et al. in view of Merrill (U.S. Patent No. 5,171,264). Herweck et al. disclose a device which can be used for stimulating the growth of eukaryotic blood cells (see Abstract and column 11, lines 24 - 49) and using this device as a "matrix and support upon which cellular matter is grown" (column 11, lines 26 - 27). This device consists of a substrate which can be manufactured from any suitable biocompatible material including fibers and polymers (see column 8, lines 44 - 57). Herweck et al. disclose that the substrate of the device can be shaped in any way needed for its required application (see column 4, lines 21 - 25). This device is also disclosed to be implantable (Abstract, line 1) and useful for treating a patient in need of cell growth (column 4, lines 39 - 40 and claim 28). Herweck et al. also disclose coating the substrate of the device with bioactive material such as platelet derived growth factor, epidermal growth factor, transforming growth factor, erythropoietin, and fibroblast growth factor (see claim 25 and column 12, lines 1 - 35). Herweck et al achieve an enhanced rate of target cell growth, i.e.

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growth of cells at the implantation site is enhanced compared to if no implantation had been made, and certain factors which can be present stimulate, i.e. enhance, endothelial cell growth (column 6, lines 23-29 and 33-36). Herweck et al. do not disclose biocompatible tethers which have one end covalently linked to the substrate and a growth effector molecule covalently linked to the other end. Merrill discloses star molecules composed of biocompatible, non-thrombogenic, water-soluble polyethylene oxide (PEO)(see Abstract and column 1, line 21) which can have one arm covalently linked to a substrate thereby anchoring the molecule (see column 2, lines 11 - 14) and another arm covalently linked to a bioactive molecule (see column 5, lines 3 - 8 and claim 15). The same tresyl chloride attachment agent can be used to attach the star molecule to the substrate and to the bioactive molecule (see, e.g., column 4, lines 7-9 and 61-64, and claims 10-16). It would have been obvious to one of ordinary skill in the art at the time applicants' invention was made to make a composition for use in stimulating the growth of eukaryotic blood cells consisting of a biocompatible substrate, biocompatible tethers and growth effector molecules as described by Herweck et al. using the polyethylene oxide star molecules for the biocompatible tether components as described by Merrill because the star molecules will prevent thrombogenesis from occurring when the device of Herweck et al. is implanted while still ensuring that the device remains coated with the bioactive material. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the tresyl chloride attachment agent of Merrill to attach the biocompatible substrate and the growth effector molecules of Herweck et al to the biocompatible tethers because Merrill discloses tresyl chloride to be a useful attachment means, and the use of tresyl chloride as the

attachment means would not have been expected to affect adversely the functioning of Herweck et al's bioactive materials.

6. Claim 17 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Herweck et al. in view of Merrill (U.S. Patent No. 5,171,264) as applied against claims 14 - 16 and 33 above, further in view of Mikos. Neither Herweck et al. nor Merrill disclose a substrate which is biodegradable. Mikos discloses a "biodegradable, bioresorbable, three-dimensional template for repair and replacement of diseased or injured bone which provides mechanical strength to bone while also providing a guide for growth of bone tissue" (see Abstract, lines 1 - 4). Mikos discloses that "the implant is seeded with osteoblasts prior to implantation to provide regeneration sites for bone tissue" (see column 1, lines 64 - 63). It would have been obvious to one of ordinary skill in the art at the time applicants' invention was made to make a cell growth composition outlined in the above rejection using a biodegradable material as described by Mikos because a patient in need of an implantable cell growth composition might only need it for a defined period of time and it would be less deleterious to the patient and more conducive to overall healing to have the cell growth composition biodegrade and be bioabsorbed so that further surgery and trauma to the patient would not be necessary.

7. Applicant's arguments filed August 27, 2003 have been fully considered but they are not persuasive.

The rejections based upon Herweck et al in view of Merrill '264, and based upon Herweck et al in view of Merrill '264 and further in view of Mikos, are maintained. Applicants contend that Herweck et al do not provide motivation for arriving at Applicants' invention because if Herweck et al and Merrill '264 were combined for the purpose of tethering and



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stimulating cell growth, this would result in clogging of the of the capillary lumina in which the devices of Herweck et al are to be implanted. The examiner disagrees. Herweck et al specifically teach that they want to encourage the growth of cells within their device (see, e.g., the Abstract; column 4, line 59 - column 5, line 14; column 6, lines 5-29 and 61-68; etc.). One of ordinary skill in the art is motivated under 35 U.S.C. 103 to act consistently with the expressly recited goals of Herweck et al. Applicants also argue that Merrill '264 only teaches uses with which cell growth is undesirable, and thus does not provide motivation for tethering growth effector molecules. However, as noted by Applicants, Merrill '264 teaches that its immobilized PEO star molecules are useful for "numerous biomedical applications (column 2, lines 17-23). The mere existence of a few incompatible specific applications does not negate motivation for other biomedical applications. Further, as the prior art is to be considered as a whole in determining obviousness, it is acceptable to rely at least in part upon the disclosure of Herweck et al to provide motivation for combining the two references.

At page 8 of the response, Applicants argue that "Herweck et al is drawn to drug delivery". This is incorrect. Herweck et al, e.g., at the Abstract; column 4, line 59 - column 5, line 14; and column 6, lines 5-29 and 61-68; disclose implantable devices in which cell growth is to be encouraged. Applicants argue that "Merrill is drawn to devices for use in bioseparations". This is incorrect. As noted by Applicants at page 7 of the remarks, Merrill is also drawn to biomedical applications such as implants (see, e.g., column 2, lines 17-23, and claims 7, 11, and 12). Applicants argue that "neither reference relates to materials for culturing cells". This is incorrect, as shown by the sections of Herweck et al cited above. Applicants argue that "one skilled in the art would not normally look to art relating to drug delivery or bioseparations for

guidance on ways to increase the rate cell growth in culture”. This is correct, but not relevant to the rejections at issue because the disclosure of Herweck et al is not limited to drug delivery, and the disclosure of Merrill ‘264 is not limited to bioseparations. Applicants argue that “Herweck does not suggest that it would be advantageous to tether growth factors to the substrate, and Merrill does not suggest using the star molecules for tethering growth effector molecules to a substrate”. This is correct, but not relevant to the rejections at issue because differences between the claims and the individual references are not determinative as to whether prima facie obviousness exists. See also the remarks at pages 5-6 of the Office action mailed October 29, 2002, and at page 22 of the Examiner’s Answer mailed January 21, 1998.

There is deemed to be motivation to combine Herweck et al, Merrill ‘264, and Mikos. Herweck and Merrill et al ‘264 are not limited drug delivery and cell separation devices. Rather, both these references, and Mikos, disclose implants, and Mikos suggests the use of a substrate material which would be useful in the implants of Herweck et al and Merrill ‘264.

The obviousness-type double patenting rejections are maintained. Applicants contend that the selection of multi-branched tethers is a difference between the instant claims and the claims of U.S. Patent No. 6,045,018. However, claims 32 and 34, which are the only claims rejected over U.S. Patent No. 6,045,018, do not recite multi-branched tethers. Claims 32 and 34 generically recite the use of polymeric tethers, which encompasses polymeric tethers. The selection of multi-branched tethers is not a claimed difference over the claims of the ‘018 patent, and therefore does not need to be addressed or resolved in the obviousness-type double patenting rejection. Applicants contend that the claims of the ‘828 patent and the ‘818 patent do not recite or suggest the important feature of orientation and spacing of the tether and the attached growth


effector molecules, and do not recite or suggest obtaining a substantially optimum activity of the growth effector molecules. However, as the instant claims do not recite any of these features, it is not relevant as to whether the claims of the '828 patent or of the '818 patent claims suggest them. Patentability must be based upon claimed, not unclaimed, differences over the reference being applied. Form Paragraph 8.36, quoted in MPEP 804, shows that secondary references may be used in support of an obviousness-type double patenting rejection. Applicants' citation to Bartfeld is not understood, as that case deals only with a §102(e)/§103 rejection, not an obviousness-type double patenting rejection. In any event, in the Longi case discussed in Bartfeld, the court stated that an obviousness-type double patenting rejection may take into account the skill of the art and prior art other than the invention claimed in the issued patent. See Longi at page 648.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

September 30, 2003